CORTICAL ACTIVITY DURING HYPOXIC HYPERVENTILATION

M. Pokorski¹, A. Trojecka¹, M. Marczak¹, A. Wierzbicka², W. Jernajczyk²

¹Department of Respiratory Research, Medical Research Center, Polish Academy of Sciences, Warsaw and ²Department of Clinical Neurophysiology, Institute of Psychiatry and Neurology, Warsaw, Poland

ABSTRACT

This study seeks to determine the pattern of electroencephalogram changes during stimulatory ventilatory responses to acute progressive hypoxia. Electroencephalograms were recorded in the 10-20 electrode system during progressive poikilocapnic hypoxic tests based on the rebreathing routine. Healthy subjects were used for the study. A major finding was that hypoxia decreased the power spectra of the alpha activity. The decrease was surprisingly rapid and greater at mild hypoxic desaturation when pulmonary ventilation was about to pick up than during the maximum hypoxic hyperventilation. The possible relation of hypoxic decline in brain bioactivity to the manifestation of hypoxic hyperventilation remains to be elucidated in further studies.

Key words: arterial oxygen saturation, cortical alpha activity, EEG, hypoxia, hyperventilation

INTRODUCTION

The first trials of recording the electroencephalographic (EEG) activity during cerebral hypoxia in humans took place as early as in the 1930s. Those and later, rather infrequent studies of the issue, rendered a picture that seems to have been one of a decrease in the alpha activity and an increase in slow EEG activity due to hypoxia (1). The decrease in the alpha activity, particularly noted in extended periods of hypoxic tests of up to 1 h (2, 3), also is a feature of respiratory pathologies associated with hypoxia, such as asthma or chronic obstructive pulmonary disease (4), and may constitute a plausible explanation for cognitive impairment (5) or increased latency of P300 (6), a positive wave occurring about 300 ms after an auditory or visual stimulus, which is considered to reflect mental processes, observed in these pathologies.

Sudden hypoxic episodes of a short duration are now recognized as being the predominant and most common form of hypoxia in a number of respiratory ailments, e.g., sleep apnea syndromes, and also on occasion in apparently healthy subjects. Such episodes are usually related to hypoxic hyperventilation, as hypoxia evokes a rapid increase in pulmonary ventilation, mediated by the carotid body chemoreceptor reflex (7). During hypoxia, therefore, one deals with two
functions of opposing kinetics, an increase in brainstem motor respiratory output running down to the diaphragm and a decrease of basal cortical activity that in fact radiates to the brainstem respiratory areas. An interaction between these two functions in awake humans is not an unreasonable assumption, but its nature is largely open to conjecture. Dampening of alpha activity may be germane for the central hypoxic ventilatory depression, a known feature of longer lasting or chronic hypoxia. A similar phenomenon has not yet been ascribed to acute hypoxia, but the possibility exists that low cortical activity could mitigate the hypoxic ventilatory increase. In the present study we addressed this issue by examining the EEG and ventilatory responses to acute progressive hypoxia in healthy subjects. We asked a question of whether there would be an association between EEG and ventilatory changes and whether any such relation would stand the extreme hyperventilation of severe hypoxia.

MATERIAL AND METHODS

The study was carried out in 3 healthy subjects, aged 24-32 years (F/M; 2/1), with approval of an institutional ethical committee. The subjects gave informed consent for the study. They were required to undergo a progressive pol kokilocapnic hypoxic test with simultaneous recording of EEG. The hypoxic test, based on a rebreathing technique (8), was performed in the supine position. The subjects breathed through a mouthpiece with a nose clip in place. After a several minutes’ period to accustom to the new way of breathing, they started to rebreathe from bag containing about 5L of room air. The tests took 4.5-5.2 min and were repeated in each subject after a 30 min interval. The end-point of the test was SaO\textsubscript{2} of 73%. The cortical EEG was recorded from 19 sites on the scalp using the international ten-twenty electrode position system. The following regional leads were evaluated: F4-C4, F3-C3, T6-O2, T5-O1, P4-O2, and P3-O1 (F, C, T, O, P stand for frontal, central, temporal, occipital, and parietal regions, respectively). Each EEG segment was split in 5 sec epochs and the alternate epochs were subjected to analysis. They were fast Fourier transformed (FFT) and averaged in the frequency domain. Individual band FFTs were then averaged for all EEG traces. The recordings were made and analyzed using ELMICO software (Poland). The frequency of potentials also was evaluated in the time domain. As a whole, the evaluation was backed by visual inspection. Arterial oxygen saturation and heart rate were monitored continuously. Data were expressed as mean ±SE.

RESULTS

All subjects completed the experiment. Repetition of tests gave reproducible results in each subject. Of the 6 EEG records, one was rejected for technical reasons. Data for the delta band were not interpreted because of artefacts that usually occurred in posterior leads towards the end of the test.

Cortical responses were detected in all bands subjected to analysis. Progressive hypoxia had the most striking influence on the spectral profile of alpha activity, which was declining by 33.1 μV/1% SaO\textsubscript{2} with the progression of desaturation in the mild 97-90% SaO\textsubscript{2} range (Fig. 1). The decline abated and
stabilized at a low level thereafter, amounting to a mere 1.2 $\mu V^2/1\%$ SaO$_2$ in the severe hypoxic range of 89-73% SaO$_2$ at the time of the ventilatory hyperventilation approaching its maximum. There also was a noticeable drop in the power spectrum variability at SaO$_2$<89%. These observations of contrastingly different kinetics of alpha activity changes seemingly separated by the 90% SaO$_2$ boundary prompted further comparative analysis of the activity data pooled in the SaO$_2$>95% and SaO$_2$<90% divisions. Changes in activity at the lower SaO$_2$ level, expressed as the percentage of the higher SaO$_2$ level, taken as baseline, for the bands and scalp regions studied are displayed in Table 1. On the whole, hypoxia affected power spectra of activity much more than its frequency. The spectra decreased for the alpha and beta and increased for the theta band. The most pronounced spectral changes concerned the alpha band. The power spectrum for this band decreased due to hypoxia most in the occipito-temporal region, where the decline amounted to 50.7 ±9.5% in the right and 31.6 ±10.1% in the left hemisphere. Concerning the alpha frequency, which was less influenced by hypoxia, its greatest hypoxic fall occurred in the frontal cortex: by 1.0 ±0.4 Hz in the left hemisphere and by 0.9 ±0.3 Hz in the right one.
**DISCUSSION**

A major finding of this study is that hypoxia had a dampening effect on the cortical activity of the alpha type in the EEG pattern of normal subjects, as assessed from the power spectral analysis. The decrease in alpha activity dominated over other changes due to hypoxia, such as a modest increase in theta activity. The corollary is that the EEG alpha activity was most susceptible to the effects of cerebral hypoxia. To this end, our study corroborates previous general findings on the hypoxia-induced changes in EEG, although noted in different study designs, which show a decrease in alpha activity as a predominant effect of hypoxia (2, 3). Furthermore, the decrease we observed did not concern the frequency of activity that fluctuated around the baseline level throughout, which also is in accordance with other reports (3). But our results are in opposition to some of the previous findings that show increases in both frequency and power spectra of alpha activity during the first 15 min of hypoxia (9). The different results may be due to hypobaric hypoxia used in that study, as opposed to normobaric hypoxia in the present study, although the nature of the difference is unclear.

It is no surprise that hypoxia, which is deficiency of oxygen supply for brain tissue metabolism, dampens the basal cortical activity. However, the time course of the alpha activity decline we observed was unexpected. Strikingly, alpha activity started declining from the very beginning of hypoxic exposure, the decline was most pronounced in the modest hypoxic range of SaO$_2$ 98-90%, when ventilation just starts to pick up, and stopped progressing thereafter in the low SaO$_2$ range of 89-73%, when there is an increasing and then maximum, usually fierce stimulation of ventilation by hypoxia. We can suggest a few speculative explanations for such a course of the alpha activity decline in regard to the possible association between the cortical activity and respiration during acute
hypoxia. One possibility is that there is no relation between the two and each, cortical activity and respiration, follows its own course in hypoxia. Anxiety alone, which may accompany hypoxic exposure, has been reported to decrease the alpha and increase the beta activity (10), the effects we dealt with in the present study. However, mutual influence and interaction between the cortical and respiratory functions are known to exist in normoxia in the awake state in humans (11, 12). Another possibility might be that the dampening of alpha activity denotes the central mitigating effect of hypoxia, descending onto the brain stem areas producing respiratory output. Such an effect could slow down the beginning increase in ventilation in response to the introduction of the hypoxic stimulus. In the latter phase, the function of the respiratory areas is markedly enhanced by rapidly increasing stimulatory input from the carotid body chemoreceptors that are excited by hypoxia (7). This stimulation could offset the inhibitory cortical influence, allowing ventilation to increase according to the metabolic requirements of the moment. Additionally, alpha activity decline could be counteracted by the increasing perception of the feeling of dyspnea, stressful feature of hypoxia, intensifying sharply with the progression of hypoxia below the 90% \( \text{SaO}_2 \) (8).

In conclusion, the limited results of this study show a rapid decline of the human brain bioactivity in response to acute hypoxia. Considering that the alpha activity, in a way, reflects intellectual and cognition-related brain potential (5, 13), the study suggests rapid changes in brain function, preceding the full-fledged hypoxic hyperventilation as a result of the carotid body-mediated chemoreflex. The nature of brain bioactivity hypoxic changes awaits further explorations.

Acknowledgments

This work was supported by the statutory budget of the Polish Academy of Sciences Medical Research Center.

REFERENCES


